Electrophysiological properties of human induced pluripotent stem cells.

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Authors: Peng Jiang, Stephanie N Rushing, Chi-wing Kong, Jidong Fu, Deborah Kuo-Ti Lieu, Camie W Chan, Wenbin Deng, Ronald A Li

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Public Summary:

Scientific Abstract:
Human embryonic stem cells (hESCs) can self-renew while maintaining their pluripotency. Direct reprogramming of adult somatic cells to induced pluripotent stem cells (iPSCs) has been reported. Although hESCs and human iPSCs have been shown to share a number of similarities, such basic properties as the electrophysiology of iPSCs have not been explored. Previously, we reported that several specialized ion channels are functionally expressed in hESCs. Using transcriptomic analyses as a guide, we observed tetraethylammonium (TEA)-sensitive (IC(50) = 3.3 +/- 2.7 mM) delayed rectifier K(+) currents (I(KDR)) in 105 of 110 single iPSCs (15.4 +/- 0.9 pF). I(KDR) in iPSCs displayed a current density of 7.6 +/- 3.8 pA/pF at +40 mV. The voltage for 50% activation (V(1/2)) was -7.9 +/- 2.0 mV, slope factor k = 9.1 +/- 1.5. However, Ca(2+)-activated K(+) current (I(KCa)), hyperpolarization-activated pacemaker current (I(f)), and voltage-gated sodium channel (Na(V)) and voltage-gated calcium channel (Ca(V)) currents could not be measured. TEA inhibited iPSC proliferation (EC(50) = 7.8 +/- 1.2 mM) and viability (EC(50) = 5.5 +/- 1.0 mM). By contrast, 4-aminopyridine (4-AP) inhibited viability (EC(50) = 4.5 +/- 0.5 mM) but had less effect on proliferation (EC(50) = 0.9 +/- 0.5 mM). Cell cycle analysis further revealed that K(+) channel blockers inhibited proliferation primarily by arresting the mitotic phase. TEA and 4-AP had no effect on iPSC differentiation as gauged by ability to form embryoid bodies and expression of germ layer markers after induction of differentiation. Neither iberiotoxin nor apamin had any function effects, consistent with the lack of I(KCa) in iPSCs. Our results reveal further differences and similarities between human iPSCs and hESCs. A better understanding of the basic biology of iPSCs may facilitate their ultimate clinical application.